Develop a cell replacement therapy for Parkinson's disease using human embryonic stem cells

Grant Award Details

Develop a cell replacement therapy for Parkinson's disease using human embryonic stem cells

Grant Type: Disease Team Planning

Grant Number: DT1-00688

Investigator:

Name:	Xianmin Zeng
Institution:	Buck Institute for Age Research
Type:	PI

Award Value: $37,161

Status: Closed

Grant Application Details

Application Title: Develop a cell replacement therapy for Parkinson's disease using human embryonic stem cells

Public Abstract:

Parkinson's disease (PD) is a devastating movement disorder caused by the death of dopaminergic neurons (a type of neurons in the central nervous system) present in the midbrain. These neurons secrete dopamine (a signaling molecule) and are a critical component of the motor circuit that ensures movements are smooth and coordinated.

All current treatments attempt to overcome the loss of these neurons by either replacing the lost dopamine, or modulating other parts of the circuit to balance this loss or attempting to halt or delay the loss of dopaminergic neurons. Cell replacement therapy (e.g. transplantation of dopaminergic neurons into the brain to replace lost cells and restore function) as proposed in this application attempts to use cells as small pumps of dopamine that will be secreted locally and in a regulated way, and will therefore avoid the complications of other modes of treatment. Indeed, cell therapy using fetal tissue-derived cells have shown varying success in multiple transplant studies. Work in the field has been limited however, partially due to the limited availability of cells for transplantation.

We believe that human embryonic stem cells (hESCs) may offer a potentially unlimited source of the right kind of cell required for cell replacement therapy. Work in our laboratories and in others has allowed us to develop a process of directing hESC differentiation into dopaminergic neurons. Parallel efforts by clinicians have identified process to implant the cells safely and to follow their behavior in human in a safe non-invasive fashion. Equally important, useful animal models for testing cell therapy have been developed and screening models for discovering novel therapeutic agents have also been established. We therefore believe that the time is right to mount a coordinated team effort such as the one we have proposed to develop a preclinical/clinical platform to treat PD.

In this proposal we seek to build a California team with both scientists and clinicians that have the potential to translate a promising idea (a cell therapy for PD) to an investigational new drug (IND) application. Our goals include: 1) Obtaining clinical grade hESCs, 2) Developing a manufacturing protocol to produce the appropriate transplantable dopaminergic neurons in a large scale under the Food and Drug Administration (FDA)-approved conditions; 3) Performing the appropriate safety tests in suitable animal models and to validate tools for noninvasive evaluation (for example by magnetic resonance imaging, MRI) of transplanted cells; and 4) Designing an IRB approved clinical trial protocol so that we can submit an IND application to the FDA.

Our proposal of developing hESC-based therapy for a currently non-curable disease (PD) meets CIRM's primary goal for the Disease Team Initiative and we believe our effort will advance cell-based therapy for PD toward the clinic.

Statement of Benefit to California:	We have proposed to assemble a team of scientists and clinicians that aim to develop a cell replacement therapy for a currently non-curable disease, Parkinson's disease, using human embryonic stem cells. We believe that this proposal includes the basic elements that are required for the translation of basic research to clinical research. We have proposed to obtain clinical grade human embryonic stem cells (cells not in contact with animal feeders, serum and proteins), optimize a manufacture protocol to produce the appropriate transplantable dopaminergic neurons in a large scale under the Food and Drug Administration (FDA)-approved conditions; perform efficacy and safety test in suitable animal models and develop tools for noninvasive animal studies (for example by magnetic resonance imaging, MRI) to track transplanted cells; and to design a clinical trial protocol. We believe these efforts not only provide a blueprint for moving Parkinson's disease towards the clinic for people suffering with the disorder but also a generalized blueprint for the development of stem cell therapy for multiple disorders including motor neuron diseases and spinal cord injury. The tools and reagents that we develop will be made widely available to Californian researchers and we will select California-based companies for commercialization of such therapies. We hope that California-based physicians will be at the forefront of developing this promising avenue of research. We expect that the money expended on this research will benefit the Californian research community and the tools and reagents we develop will help accelerate the research of our colleagues in both California and worldwide.